

REMARKS

The Applicants have carefully studied the outstanding Office Action. The present submission is intended to be fully responsive to the rejection raised by the Office Action and is believed to place the application in condition for allowance. Further, the Applicants do not acquiesce to any of the Office Action rejections not particularly addressed. Favorable reconsideration and allowance of the application is respectfully requested.

Claimed Status

The application as filed contained 20 claims. Of these, claims 1, 14 and 20 are in independent format. Claims 2-13 ultimately depend from claim 1, and claims 15-19 ultimately depend from claim 14. Each of the dependent claims necessarily includes all the elements from the base claims and any intervening claims.

The Applicants have amended claims 14 and 20 to attend to minor grammatical issues and not for the purpose of narrowing the claims for patentability. In addition, the Applicants have amended claim 10 to properly depend from claim 12. Please note, however, that upon favorable consideration of this claim, the Applicants request a renumbering of the claims to accommodate this change. No new matter has been added. Further, the Applicants submit that no additional fee is due because the total amount of claims fall within the allowed number of claims covered by the filing fee.

The Office Action has objected to claims 14 and 35. The Applicants note, however, that the Application as filed does not include a claim 35. Therefore, the Applicants cannot respond to such objection. With respect to the objection of claim 14, the Office Action states that in line 14 of the claim "for" should read "from." Instead of addressing this objection under a separate heading, the Applicants note that the term "for" is correct. In other words,

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the claimed element "identifying variables which affect chiral selectivity for the separation of racemic mixtures" is proper.

In addition to the aforementioned objections, the Office Action rejected claim 11 under 35 U.S.C. § 112 because the element "first frit and second frit" lack antecedent basis. The Office Action also rejected claims 1-20 under 35 U.S.C. § 103(e) as being as being unpatentable over U.S. Patent No. 5,422,004 granted to Armstrong ("Armstrong") in view of U.S. Patent No. 5,684,711 granted to Agrafiotis et al. ("Agrafiotis").

DISCUSSION

The Examiner Did Not Provide a Complete Action Pursuant to 35 C.F.R. §

1.104(c)(2)

The Office Action's grounds for rejection are not sufficiently detailed to allow the Applicants to provide a meaningful reply, and as such, the Applicants respectfully submit that the Office Action is not sufficient. In rejecting claims on grounds of anticipation or obviousness, the Examiner must cite the best references at his or her command, and when a reference is complex or shows or describes inventions other than that claimed by the applicant, the particular part relied on must be designated as nearly as practicable. 35 C.F.R. § 1.104(c)(2) (emphasis added). Further, the pertinence of each reference, if not apparent, must be clearly explained and each rejected claim specified. *Id.*

Beyond citing 35 U.S.C. § 103(a) form paragraphs, the Office Action's entire rejection of independent claims 1, 14 and 20, which comprise multiple-element claims, consists of the following vague statements:

- (1) "Armstrong teaches to identify physical variables that affect chiral selectivity for the separation of racemic mixtures, one being stationary phases."

- (2) "He teaches to determine a range of values of the physical variables."
- (3) "He teaches a finite number of experimental tests."
- (4) "He teaches a plurality of stationary phases and a plurality of collection tubes."
- (5) "He teaches assigning the test stationary phase to a particular well dispensing the racemic mixture solution into each of the stationary phases at a predetermined concentration, allowing the racemic mixture to pass through each stationary phase and collecting the solution in its corresponding tube."
- (6) "With regard to claims 1, 14 and 20, Armstrong does not teach automatically generating suggested parameters for future experiments using a computer, wherein the parameters are chosen from a new range of values based on the analysis of the plurality of racemic solutions collected."
- (7) "Agrafiotis et al. do teach automatically generating suggested parameters for future experiments using a computer, wherein the parameters are chosen from a new range of values based on the analysis of the plurality of solutions collected (see whole document, specifically Figs. 2-3)."
- (8) "One of ordinary skill in the art at the time the invention was made would have been motivated to apply Agrafiotis' method of automation with Armstrong's method for comparing chiral stationary phases in order to evaluate a greater number of stationary phases more efficiently. Agrafiotis et al. state that an automated system provides more efficient evaluation of a plurality of structure-activity models in parallel. (col. 4 lines 11-13)."
- (9) "It would have been prima facie obvious to apply Agrafiotis' automation to Armstrong's method for evaluating chiral stationary phases to achieve the expected advantage of greater efficiency in evaluating large numbers of chiral stationary phases in parallel."

Although the Office Action has seen fit to designate the particular part of *Agrafiotis* relied upon, the Office Action has not designated any part (much less the particular part) relied on nor clearly explained the pertinence of the extremely complex (e.g., 34-column, 31-example) *Armstrong* reference for any of the independent claims. Without a basis for the rejections, the Applicants cannot give a proper and complete reply. Consequently, the Applicants respectfully submit that the Office Action has failed to provide a valid action under 35 C.F.R. § 1.104(c)(2).

Section 112 Rejections

Responsive to the rejection of claim 11 under 35 U.S.C. 112, second paragraph, the Applicants submit that the claim 11 particularly points out and distinctly claims the subject matter which the Applicants regard as their invention. The element "first frit and second frit" in line 3 of the claim is not as suggested by the Office Action. Claim 11 clearly recites:

"wherein the step of packing the test stationary phases into the particular wells of the stationary phase plate includes packing the stationary phases into each well of the stationary phase plate sandwiched with a first frit and a second frit" (emphasis added).

In view of the foregoing, the Applicants submit that claim 11 does not lack antecedent basis as suggested by the Office Action. Consequently, the Applicants submit that the rejection of claim 11 under 35 U.S.C. 112, second paragraph, is unwarranted, and therefore, submit that this claim is allowable.

Claimed Invention

Pending independent claim 1 is directed to a method for separation of racemic mixtures using a synthesizer, an analyzer and a computer. And pending independent claims 14 and 20 are directed to a method for optimizing a chiral resolution using a synthesizer, an analyzer and a computer. Each of these claims includes a claimed element "providing a plurality of wells in a stationary phase plate, and a plurality of wells in a collection plate provided under the stationary phase plate."

The dependent claims 2-13 and 15-19 necessarily include the elements of the independent claims from which they depend. Thus, all of the claims include the claimed element "providing a plurality of wells in a stationary phase plate, and a plurality of wells in a collection plate provided under the stationary phase plate."

SECTION 103 REJECTIONS

As noted, the Office Action rejected claims 1-20 under 35 U.S.C. § 103(a) as being unpatentable over *Amstrong* in view of *Agrafiotis*. The Applicants respectfully traverse the Office Action rejections of these claims based on the following arguments.

Response to Section 103(a) Rejection of Claims 1-20

According to M.P.E.P. § 2143, in order to establish the required prima facie case of obvlousness of a claimed invention by applying a combination of references, (1) the proposed combination must teach or suggest all of the elements of the claimed invention, (2) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, and (3) the references must expressly or impliedly suggest the claimed invention.

(i) The Proposed Combination Does Not Teach All the Elements

The Applicants submit that neither the *Amstrong* nor *Agrafiotis* references expressly or impliedly teach or suggest all the elements of the originally-filed claims. Specifically, the Applicants submit that unlike the present claims, neither *Amstrong* nor *Agrafiotis*, alone or combined, teach the element of the presently claimed invention "providing a plurality of wells in a stationary phase plate, and a plurality of wells in a collection plate provided under the stationary phase plate."

The Applicants note that the Office Action does not rely on *Agrafiotis* for teaching this element, but instead relies on *Amstrong* to disclose such element. The Applicants, however, submit that *Agrafiotis* does not teach or suggest the claimed element.

As noted above, because the Office Action fails to designate the particular part of *Amstrong* that teaches such element, the Applicants are at a loss in replying. Nonetheless, the Applicants submit that *Amstrong* does not teach the claimed element "providing a plurality of wells in a stationary phase plate, and a plurality of wells in a collection plate provided under the stationary phase plate."

The Applicants also note that the Office Action impermissibly ignored claim terms, and thus, has not appreciated the invention as claimed. Without such appreciation, the Examiner has cited references that, alone or combined, do not teach or suggest, explicitly or inherently, the claimed invention. The Applicants submit that the Office Action merely states that *Amstrong* teaches "a plurality of stationary phases and a plurality of collection tubes." This is not the same as "providing a plurality of wells in a stationary phase plate, and a plurality of wells in a collection plate provided under the stationary phase plate."

Even with an assumption that the Office Action statement and the claimed element are the same, the Applicants submit that *Amstrong* does not discuss a plurality of wells in a stationary phase plate, much less a plurality of wells in collection plate provided under the stationary phase plate. In fact, the Applicants submit that *Amstrong* does not disclose any multi-welled, two-part system, but merely discloses (i) an individual column made from stainless steel that houses both the stationary phase and the analyte for use in liquid chromatography (e.g., Examples 2-10, 28-29 and 31), (ii) an individual capillary tube for use in electrophoresis, wherein the capillary tube impregnated with the stationary phase and wherein the analyte is forced through the impregnated capillary tube using electromigration or hydrostatic-migration injection (e.g., Examples 11-18 and 24-27, and col. 25, line 50 to col. 26, line 53), and (iii) an individual sample chamber as shown in Figure 7 for use in

absorption bubble technology, wherein the analyte is forced through the stationary phase loaded in the individual sample chamber so as to cause the one of the enantiomers of the analyte to form into a foam, reconstitute into liquid, and then be collected into a individual container (e.g., Figure 7 and col. 33, lines 5-24). Consequently, the Applicants submit that *Amstrong* fails to disclose the claimed element "providing a plurality of wells in a stationary phase plate, and a plurality of wells in a collection plate provided under the stationary phase plate."

By "providing a plurality of wells in a stationary phase plate, and a plurality of wells in a collection plate provided under the stationary phase plate" the presently claimed invention can allow an analyte to pass through the stationary phases in the wells in the stationary phase plate and collect into the corresponding wells in the collection plate. This configuration simplifies evaluating of the analytes because (i) the plurality of wells in the stationary phase plate and the underlying collection plate allow for the reduction of the number of steps in processing the samples (contrary to the multistage, complicated processing procedures set forth throughout *Amstrong*), and (ii) the collection plate or the samples contained therein can be directly fed into an analyzer, thereby preventing the processing of individual experiments caused by using an individual column, capillary or sample chamber. See the present application at pages 27-32.

Given that (1) the base reference (i.e., *Amstrong*) does not disclose explicitly or inherently the claimed element "providing a plurality of wells in a stationary phase plate, and a plurality of wells in a collection plate provided under the stationary phase plate," and (2) the second reference (i.e., *Agrafiotis*) is not cited for and also fails to disclose such subject matter, the Applicants submit that these references either alone or combined, fail to disclose

or suggest, all of the claimed elements. In light of the foregoing, the Applicants respectfully submit that the Office Action has failed to raise a *prima facie* case of obviousness with respect to the independent claims 1, 14 and 20.

Since the dependent claims necessarily include the elements of the independent claims from which they depend, each of the dependent claims includes the above-listed elements of the independent claims from which they depend. Thus, the Applicants submit that the Office Action has failed to raise a *prima facie* case of obviousness with respect to the dependent claims.

(ii) Failure to Provide an Objective Reason to Combine References

In addition to other requirements, in order to establish the required *prima facie* case of obviousness of a claimed invention by applying a combination of references, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. See M.P.E.P. § 2143.01.

In addition, "a statement that modifications of the prior art to meet the claimed invention would have been 'well within the ordinary skill of the art at the time the claimed invention was made' because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references." *Id.*

With respect to dependent claims 1-20, the Applicants respectfully submit that the Office Action has not provided a legitimate reference or statement showing some suggestion

of the desirability of doing what the Applicants have done. The Office Action, without providing any reference or convincing reasoning and using impermissible hindsight and language paralleling the above-quoted language held to be insufficient to establish a *prima facie* case of obviousness, stated:

"[o]ne of ordinary skill in the art at the time the invention was made would have been motivated to apply Agrafiotis' method of automation with Armstrong's method for comparing chiral stationary phases in order to evaluate a greater number of stationary phases more efficiently; and

[i]t would have been *prima facie* obvious to apply Agrafiotis' automation to Armstrong's method for evaluating chiral stationary phases to achieve the expected advantage of greater efficiency in evaluating large numbers of chiral stationary phases in parallel."

Although the Office Action states that Agrafiotis states "that an automated system provides more efficient evaluation of a plurality of structure-activity models in parallel. (col. 4 lines 11-13)." This statement does not provide a suggestion or motivation to combine the teachings of Armstrong and Agrafiotis to obtain the Applicants' invention. In other words, the automated system of Agrafiotis provides a more efficient method to evaluate a plurality of structure-activity models in parallel and not to evaluate analytes in a plurality wells. The Applicants direct the Examiner to Agrafiotis at col. 3, line 30 to col. 4, line 4 (reproduced below), which clearly shows that Agrafiotis' method to evaluate a plurality of structure-activity models in parallel and is in no way related to efficiently evaluating analytes in a plurality wells. As set forth in Agrafiotis:

"the present invention is directed to an iterative process for generating new chemical compounds with a prescribed set of physical, chemical and/or biological properties, and to a system for implementing this process. During each iteration of the process, (1) a directed diversity chemical library is robotically generated in accordance with robotic synthesis instructions; (2) the compounds in the directed diversity chemical library are

analyzed under computer control, and structure-activity/structure-property models (collectively referred to as structure-activity models hereafter) are constructed and/or refined; and (3) new robotic synthesis instructions are generated to control the synthesis of the directed diversity chemical library for the next iteration.

More particularly, during each iteration of the process, the system of the present invention robotically synthesizes, in accordance with robotic synthesis instructions, a directed diversity chemical library comprising a plurality of chemical compounds. The chemical compounds are robotically analyzed to obtain structure-activity/structure-property data (collectively referred to as structure-activity data hereafter) pertaining thereto. The structure-activity data is stored in a structure-activity/structure-property database (referred to as structure-activity database hereafter). The structure-activity database also stores therein structure-activity data pertaining to previously synthesized compounds.

The system of the present invention evaluates, under computer control, the structure-activity data of the chemical compounds obtained from all previous iterations (or a subset of all previous iterations as specified by user input, for example) and constructs structure-activity models that substantially conform to the observed data." Agrafiotis at col. 3, line 30 to col. 4, line 4 (emphasis added).

Therefore, the Applicants submit that the above-noted motivation-to-combine statement in the Office Action does provide a suggestion or motivation to combine the teachings of *Amstrong* and *Agrafiotis* to:

- automatically generat[e] suggested parameters for future experiments using the computer wherein the suggested parameters are chosen from a new range of values, and wherein automatically generating the suggested parameters is based on the analysis of the racemic solutions collected in the plurality of wells in the collection plate; (claim 1)
- automatically generat[e] a statistical analysis using the computer based on the step of determining the magnitude of chiral resolution and at least one of the variables identified in order to evaluate the chiral resolution in the wells; and automatically generate, using the computer, suggested parameters for future experiments based on the statistical analysis; (claim 14) and
- automatically generat[e] a statistical analysis using the computer based on the step of determining the magnitude of chiral resolution and the test stationary phases in order to evaluate the chiral resolution in the wells; and automatically generate, using the computer, suggested stationary phases for future experiments based on the statistical analysis, wherein

the suggested stationary phases are selected from the library of potential stationary phases and being different from the test stationary phases.

In addition, as used by the Office Action, combining the references for the purpose of "evaluating a greater number of stationary phases more efficiently" does not provide a suggestion or motivation to combine the teachings of *Amstrong* and *Agrafiotis* to obtain the Applicants' invention. Specifically, simply stating that the combination allows for "evaluating a greater number of stationary phases more efficiently" does not point to combining the supposed elements contained in *Amstrong* and the supposed elements contained in *Agrafiotis* to obtain the Applicants' invention. Thus, the Office Action has not provided a well-reasoned basis for the combination. Moreover, "evaluating a greater number of stationary phases more efficiently" does not show how the teachings of *Amstrong* can be combined with teachings *Agrafiotis* to produce the claimed invention.

At most, "evaluating a greater number of stationary phases more efficiently" provides a reason for applying for a patent in the first place. That is, many patentable inventions are based on the recognition that a specific combination of elements (which appear individually, but not in combination, in the prior art) will result in an improved system.

Thus, because of the absence of any evidence of a motivating force, the Applicants submit that the Office Action has failed to meet the initial burden of providing a *prima facie* case of obviousness. The Applicants submit therefore that claims 1-20 are allowable.

(iii) The References Do Not Expressly or Impliedly Suggest the Claimed Invention

Under 35 U.S.C. § 103, to support the conclusion that the claimed invention is directed to obvious subject matter, the combination of references must expressly or impliedly suggest the claimed invention. The Applicants submit that *Amstrong* and *Agrafiotis*,

alone or combined, fail to expressly or impliedly teach or suggest the claimed invention of claims 1-20.

Despite the Office Action ignoring claim terms, the Applicants assume for the sake of argument that the Office Action cites *Amstrong* for the proposition that it "discloses providing a plurality of wells in a stationary phase plate, and a plurality of wells in a collection plate provided under the stationary phase plate." The Office Action nonetheless acknowledges that *Amstrong* does not disclose "does not teach automatically generating suggested parameters for future experiments using a computer, wherein the parameters are chosen from a new range of values based on the analysis of the plurality of racemic solutions collected." The Office Action instead relies on *Agrafiotis* for the proposition that it teaches "automatically generating suggested parameters for future experiments using a computer, wherein the parameters are chosen from a new range of values based on the analysis of the plurality of racemic solutions collected."

Contrary to the Office Action's assertions, combining *Amstrong* and *Agrafiotis* does not morph into what the Applicants have done. To this end, the Applicants submit that *Amstrong* does not disclose a multiple-well, two-part system (i.e., the stationary-phase and collection plates) for analyzing analytes, but rather, only an individual column, an individual capillary tubes and an individual sample chamber for analyzing analytes. *Agrafiotis* teaches automated system that provides for evaluating of a plurality of structure-activity models in parallel. And as noted above, the structure-activity models are constructs of structure-activity data of the chemical compounds obtained from evaluating one or more analytes.

Thus, if one were to combine *Amstrong* and *Agrafiotis*, the resulting combination may be a system that uses *Agrafiotis*' method for evaluating a plurality of structure-activity models

in parallel for each individual test carried out by the method of *Amstrong*. The Applicants submit, however, that such combination would not be the method of claims 1, 14 and 20.

That is, the resulting combination, for example, would not be the method of claim 1, which (i) provides a plurality of wells in a stationary phase plate and plurality of wells in a collection plate provided under the stationary phase plate; (ii) allows an analyte to pass through the stationary phases and collect into the corresponding wells in the collection plate; (iii) analyzes, using the analyzer, the analyte collected in the plurality of wells in the collection plate; and (iv) automatically generates suggested parameters for future experiments using the computer wherein the suggested parameters are chosen from a new range of values, and wherein the automatically generation is based on the analysis of the analyte collected in the plurality of wells in the collection plate.

In view of the foregoing, the Applicants submit that the combination of *Amstrong* and *Agrafiotis*, either alone or combined, fails to teach or suggest the claimed invention of independent claims 1, 14 and 20. Since the dependent claims necessarily include the elements of the base claims from which they depend, the dependent claims 2-13 and 15-19 are allowable for the same reasons. Therefore, the Applicants respectfully submit that the Examiner has failed to make a *prima facie* case of obviousness.

CONCLUSION


The Applicants submit that the application is in good and proper form for allowance and respectfully request the Examiner to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of this application, the Examiner is invited to call the undersigned attorney, at 312-913-3304.

Respectfully submitted,

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